1

Appl. No. 09/939,230 Amdt. dated 3/23/2005 Reply to Office Action of August 25, 2004

This listing of claims will replace all prior versions, and listings of claims in the application:

## **Listing of Claims**

## 1-44. (Canceled)

- 45. (Original) A method for reducing anxiety in a subject in need thereof by increasing ion flow through KCNQ potassium channels in a cell, the method comprising the step of administering to the subject a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound able to increase ion flow through KCNQ potassium channels, said composition administered to the subject in a potassium channel-opening amount, thereby reducing anxiety in the subject.
- 46. (Original) The method of claim 45, wherein the anxiety is caused by panic disorder, generalized anxiety disorder, or stress disorder.
- 47. (Original) The method of claim 46, wherein the stress disorder is acute stress disorder or post-traumatic stress disorder.
  - 48. (Original) The method of claim 45, wherein the subject is a human.
- 49. (Original) The method of claim 45, wherein the KCNQ channel is a heteromeric channel.
- 50. (Original) The method of claim 45, wherein the KCNQ channel is a homomeric channel.
- 51. (Previously Presented) The method of claim 49, wherein the heteromeric KCNQ channel comprises a KCNQ2 polypeptide subunit.
- 52. (Previously Presented) The method of claim 49, wherein the heteromeric KCNQ channel comprises a KCNQ3 polypeptide subunit.

Appl. No. 09/939,230 Supplemental Amdt. dated 3/22/05 Reply to Office Action of August 25, 2004

- 53. (Original) The method of claim 52, wherein the KCNQ channel is KCNQ2/3.
- 54. (Original) The method of claim 45, wherein the potassium channel-opening amount is 0.1 mg/kg to 200 mg/kg.
- 55. (Original) The method of claim 54, wherein the potassium channel-opening amount is 10 mg/kg to 100 mg/kg.
- 56. (Original) The method of claim 45, wherein the composition is administered orally.
- 57. (Original) The method of claim 45, wherein the composition is administered by injection.
- 58. (Original) The method of claim 45, wherein the compound able to increase ion flow through KCNQ potassium channels has the formula:

$$Ar^1$$
 $N$ 
 $Ar^2$ 

wherein

Ar<sup>1</sup> and Ar<sup>2</sup> are each members independently selected from the group consisting of aryl, substituted aryl, heteroaryl and substituted heteroaryl; and X is a member selected from the group consisting of O, S and N-R<sup>1</sup>, wherein R<sup>1</sup> is a member selected from the group consisting of H, (C<sub>1</sub>-C<sub>8</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>8</sub>)alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C<sub>1</sub>-C<sub>4</sub>)alkyl, substituted aryl(C<sub>1</sub>-C<sub>4</sub>)alkyl, CN, -C(O)R<sup>2</sup>, -OR<sup>3</sup>, -C(O)NR<sup>3</sup>R<sup>4</sup>, and -S(O)<sub>2</sub>NR<sup>3</sup>R<sup>4</sup>;

- wherein  $R^2$  is a member selected from the group consisting of  $(C_1-C_8)$ alkyl, substituted  $(C_1-C_8)$ alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl $(C_1-C_4)$ alkyl and substituted aryl $(C_1-C_4)$ alkyl; and
- R<sup>3</sup> and R<sup>4</sup> are each members independently selected from the group consisting of hydrogen, (C<sub>1</sub>-C<sub>8</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>8</sub>)alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C<sub>1</sub>-C<sub>4</sub>)alkyl and substituted aryl(C<sub>1</sub>-C<sub>4</sub>)alkyl, or R<sup>3</sup> and R<sup>4</sup> can be combined with the nitrogen to which each is attached to form a 5-, 6- or 7-membered ring optionally having additional heteroatoms at the ring vertices.
- 59. (Previously Presented) The method according to claim 58, wherein Ar<sup>1</sup> is a member selected from the group consisting of phenyl, substituted phenyl, indolyl, substituted indolyl, benzofuranyl, substituted benzofuranyl, furanyl, substituted furanyl, thienyl, substituted thienyl, isothiazolyl, substituted isothiazolyl, pyrazolyl and substituted pyrazolyl.
- 60. (Previously Presented) The method according to claim 58, wherein Ar<sup>1</sup> is substituted phenyl, substituted or unsubstituted 2-indolyl and substituted or unsubstituted 2-thienyl.
  - 61. (Original) The method according to claim 58, wherein X is O.
- 62. (Original) The method according to claim 60, wherein the  $Ar^1$  substituents are selected from the group consisting of halogen, alkyl, halo( $C_1$ - $C_4$ )alkyl, ( $C_1$ - $C_4$ )alkoxy, halo( $C_1$ - $C_4$ )alkoxy, nitro, cyano, -NHC(O) $R^7$ , -NHR $^7$ , phenyl and substituted phenyl, wherein

 $R^7$  is a member selected from hydrogen,  $(C_1-C_8)$ alkyl, substituted  $(C_1-C_8)$ alkyl, cycloalkyl, substituted cycloalkyl, heteroalkyl, substituted heteroalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl $(C_1-C_4)$ alkyl and substituted aryl $(C_1-C_4)$ alkyl, or  $R^7$  can be combined with the nitrogen to which it is attached to form a 5-, 6- or 7-membered ring optionally having additional heteroatoms at the ring vertices.

Appl. No. 09/939,230 Supplemental Amdt. dated 3/22/05 Reply to Office Action of August 25, 2004

- 63. (Previously Presented) The method according to claim 58, wherein Ar<sup>2</sup> is selected from the group consisting of heteroaryl and substituted heteroaryl.
- 64. (Original) The method according to claim 58, wherein Ar<sup>1</sup> is substituted aryl; Ar<sup>2</sup> is heteroaryl or substituted heteroaryl; and X is O.
- 65. (Original) The method according to claim 62, wherein Ar<sup>2</sup> is pyridyl or substituted pyridyl.
- 66. (Original) The method according to claim 65, wherein Ar<sup>2</sup> is selected from the group consisting of 6-methyl-3-pyridyl and 2-chloro-5-pyridyl.
- 67. (Original) The method according to claim 65, wherein Ar<sup>1</sup> is substituted phenyl.
- 68. (Original) The method according to claim 67, said compound having the formula:

wherein,

Y is a member selected from the group consisting of halogen,  $C_1$ - $C_4$  alkyl,  $C_1$ - $C_4$  substituted alkyl, -OCH<sub>3</sub> and -OCF<sub>3</sub>, and  $R^5$  and  $R^6$  are members independently selected from the group consisting of H, halogen, alkyl, halo( $C_1$ - $C_4$ )alkyl, nitro, cyano and phenyl, with the proviso that both  $R^5$  and  $R^6$  are not H.

69. (Original) The method according to claim 68, wherein R<sup>5</sup> and R<sup>6</sup> are members independently selected from the group consisting of H, F, and Cl, with the proviso that both R<sup>5</sup> and R<sup>6</sup> are not H.

70. (Original) The method of claim 45, wherein the compound able to increase ion flow through KCNQ potassium channels has the formula:

wherein

- R<sup>1</sup> is a member selected from the group consisting of substituted or unsubstituted branched (C<sub>3</sub>-C<sub>8</sub>)alkyl, substituted or unsubstituted (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;
- R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are each members independently selected from the group consisting of hydrogen, fluorine and substituted or unsubstituted (C<sub>1</sub>-C<sub>8</sub>)alkyl, or optionally any two of R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are joined together to form a three- to seven-membered ring, having from 0 to 3 heteroatoms as ring members, or R<sup>2</sup> and R<sup>4</sup> taken together form a second bond between the carbon atoms to which each is attached, or R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> taken together represent a second and third bond between the carbon atoms to which each is attached;
- R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each members independently selected from the group consisting of hydrogen, fluorine and substituted or unsubstituted (C<sub>1</sub>-C<sub>8</sub>)alkyl, or optionally any two of R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are joined together to form a three- to seven-membered ring, having from 0 to 3 heteroatoms as ring members;
- R<sup>10</sup> is a member selected from the group consisting of substituted or unsubstituted (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl, substituted or unsubstituted (C<sub>3</sub>-C<sub>8</sub>)heterocycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

X is a member selected from the group consisting of O, S and N-R<sup>11</sup>, wherein R<sup>11</sup> is a member selected from the group consisting of H, (C<sub>1</sub>-C<sub>8</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>8</sub>)alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C<sub>1</sub>-C<sub>4</sub>)alkyl, substituted aryl(C<sub>1</sub>-C<sub>4</sub>)alkyl, -CN, -C(O)R<sup>12</sup>, -OR<sup>13</sup>, -NR<sup>13</sup>R<sup>14</sup>, -C(O)NR<sup>13</sup>R<sup>14</sup>, and -S(O)<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>; wherein R<sup>12</sup> is a member selected from the group consisting of (C<sub>1</sub>-C<sub>8</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>8</sub>)alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C<sub>1</sub>-C<sub>4</sub>)alkyl and substituted aryl(C<sub>1</sub>-C<sub>4</sub>)alkyl; and

R<sup>13</sup> and R<sup>14</sup> are each members independently selected from the group consisting of hydrogen, (C<sub>1</sub>-C<sub>8</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>8</sub>)alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C<sub>1</sub>-C<sub>4</sub>)alkyl and substituted aryl(C<sub>1</sub>-C<sub>4</sub>)alkyl, or R<sup>13</sup> and R<sup>14</sup> can be combined with the nitrogen to which each is attached to form a 5-, 6- or 7-membered ring optionally having additional heteroatoms at the ring vertices; and

m, n, p and q are each independently an integer of from 0 to 1, with the proviso that at least one of m, n, p or q is 1.

- 71. (Original) The method of claim 70, wherein X of the compound is O.
- 72. (Original) The method of claim 70, wherein m and n of the compound are zero.
- 73. (Original) The method of claim 70, wherein m of the compound is 1 and n of the compound is zero.
- 74. (Original) The method of claim 70, wherein m and n of the compound are each 1.

- 75. (Original) The method of claim 70, wherein m and p of the compound are each zero, and n and q of the compound are each 1.
- 76. (Original) The method of claim 70, wherein m, n, p and q of the compound are each 1.
- 77. (Previously Presented) The method of claim 70, wherein R<sup>2</sup> and R<sup>4</sup> of the compound, taken together, form a second bond joining the carbon atoms to which each is attached.
- 78. (Previously Presented) The method of claim 70, wherein m and p of the compound are each 1,  $R^2$ ,  $R^3$ ,  $R^6$  and  $R^7$  of the compound are each hydrogen, n and q of the compound are each zero, and  $R^{10}$  of the compound is selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl.
- 79. (Previously Presented) The method of claim 78, wherein R<sup>10</sup> of the compound is substituted aryl having from one to three substituents selected from the group consisting of halogen, halo(C1-C4)alkyl, halo(C1-C4)alkoxy, (C1-C4)alkyl, (C1-C4)alkoxy, nitro, cyano, phenyl and methylenedioxy.
- 80. (Previously Presented) The method of claim 70, wherein m, n, p and q of the compound are each 1, and R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> of the compound are each hydrogen.
- 81. (Previously Presented) The method of claim 70, wherein m, n, p and q of the compound are each 1; R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> of the compound are each hydrogen; and R<sup>10</sup> of the compound is selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl.
- 82. (Previously Presented) The method of claim 81, wherein R<sup>1</sup> of the compound is selected from the group consisting of substituted or unsubstituted branched (C3-C8)alkyl, and substituted or unsubstituted (C3-C8)cycloalkyl.